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<110> REGENERON PHARMACEUTICALS, INC.
      <120> RECEPTOR BASED ANTAGONISTS, AND METHODS OF MAKING
            AND USING
      <130> REG 203-A
      <140> USSN 09/313,942
      <141> 1999-05-19
      <150> 09/313,942
      <151> 1999-05-19
      <150> 60/101,858
      <151> 1998-09-25
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      <213> Artificial Sequence
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      <223> Tag sequence
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His His His His His
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1
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<210> 4 <211> 10

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Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
                                25
                                                     30
Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
                            40
Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
                        55
Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
                                         75
                    70
Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
                                    90
                85
Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
                                 105
Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
                            120
Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
    130
                        135
Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
                    150
                                         155
Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg
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Asp	Thr	Pro	Thr	165 Ser	Cys	Thr	Val		170 Tyr	Ser	Thr	Val		175 Phe	Val				
Asn	Ile	Glu	180 Val	Trp	Val	Glu		185 Glu	Asn	Ala	Leu		190 Lys	Val	Thr				
Ser			Ile	Asn	Phe		200 Pro	Val	Tyr	Lys		205 Lys	Pro	Asn	Pro		•		
	210 His		Leu	Ser		215 Ile	Asn	Ser	Glu		220 Leu	Ser	Ser	Ile					
225 Lys	Leu	Thr	Trp		230 Asn	Pro	Ser	Ile		235 Ser	Val	Ile	Ile		240 Lys				
Tyr	As'n	Ile	Gln 260	245 Tyr	Arg	Thr	Lys	Asp 265	250 Ala	Ser	Thr	Trp	Ser 270	255 Gln	Ile				
Pro	Pro	Glu 275	Asp	Thr	Ala	Ser	Thr 280		Ser	Ser	Phe	Thr 285		Gln	Asp				
Leu	Lys 290	Pro	Phe	Thr	Glu	Tyr 295		Phe	Arg	Ile	Arg 300		Met	Lys	Glu				
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385	_	Leu	Thr	vaı	390	пеи	TIIT	WOII	ASP	395	тут	TIELL	Аια	TIIT	400				
Thr	Val	Arg	Asn	Leu 405	Val	Gly	Lys	Ser	Asp 410	Ala	Ala	Val	Leu	Thr 415	Ile				
			Asp 420					425					430						
		435	Asp		,		440					445							
	450	-	Lys Thr			455					460								
465		TT-2	1111	_	470	GTII	GTII	GIU	Asp	475	1114	vaı	птэ	MT 9	480				
_			Gly	485					490					495					
			Tyr 500					505					510						
_		515	Gln Lys				520					525							
	530		Asn			535					540								
.545			Asn		550					555			1		560				
			Ser	565					570				Val	575					
Ala	Ala		580 Thr		Glu	Gly		585 Lys	Asp	Gly	Pro		590 Phe	Thr	Phe				
Thr			Lys	Phe	Ala	Gln 615	600 Gly	Glu	Ile	Glu	Ser 620	605 Gly	Glu	Pro	Lys				
Ser 625			Lys	Thr	His 630	Thr	Cys	Pro	Pro	Cys 635		Ala	Pro	Glu	Leu 640				
		Gly	Pro	Ser 645			Leu	Phe	Pro 650	Pro	Lys	Pro	Lys	Asp 655					

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val 680 Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser 695 Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu 710 715 Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala 730 725 Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro 740 745 Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln 760 Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala 775 Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr 790 795 Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu 805 810 Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser 820 825 830 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser 835 840 845 Leu Ser Pro Gly Lys His His His His His 850 855

<210> 8 <211> 592

<212> PRT

<213> Homo sapiens

## <400> 8

Met Val Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro 10 Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg 20 25 Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro 40 Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys 55 Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys 90 85 Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val 100 105 Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser 115 120 Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr 135 Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys 165 170 Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met 185 180 190 Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe 200 205 Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val 215

Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp 230 235 Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg 245 250 Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp 260 265 Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His 280 285 Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser 295 300 Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser 310 315 Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr 330 325 Asn Lys Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr 345 Ser Leu Pro Val Gln Asp Ala Gly Glu Pro Lys Ser Cys Asp Lys Thr 360 365 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser 375 380 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 3.90 395 Thr Pro Glu Val Thr Cys Val Val Asp Val Ser His Glu Asp Pro 405 410 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 425 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val 435 440 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 455 460 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr 470 475 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 485 490 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys 500 505 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser 520 525 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp 535 540 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser 550 555 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala 570 565 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 580 585

<210> 9

<211> 951

<212> PRT

<213> Homo sapiens

<400> 9

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 10
 15

 Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
 20
 25
 30

 Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
 35
 40
 45

 Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
 50
 60

Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys Tyr Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser Thr Trp Ser Gln Ile Pro Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser Phe Thr Val Gln Asp Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile Thr Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser Phe Trp Tyr Lys Ile Asp Pro Ser His Thr Gln Gly Tyr Arg Thr Val Gln Leu Val Trp Lys Thr Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile Leu Asp Tyr Glu Val Thr Leu Thr Arg Trp Lys Ser His Leu Gln Asn Tyr Thr Val Asn Ala Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Leu Ala Thr Leu Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile Pro Ala Cys Asp Phe Gln Ala Thr His Pro Val Met Asp Leu Lys Ala •425 Phe Pro Lys Asp Asn Met Leu Trp Val Glu Trp Thr Thr Pro Arg Glu Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala Pro Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly Thr Val His Arg Thr Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser Ile Lys Ala Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val Arg Thr Lys Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln Leu Pro Val Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe Tyr Arg Thr

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550
                                        555
Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser His Thr Glu
                565
                                    570
Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met Val Arg Met
            580
                                585
Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu Phe Thr Phe
                            600
Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ser Gly Ala Ser Thr
                        615
                                            620
Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
                    630
                                        635
Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
                645
                                    650
Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
            660
                                665
                                                    670
Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
                            680
                                                685
Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
                        695
                                            700
Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
                   710
                                        715
Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
                725
                                    730
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            740
                                745
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        755
                            760
                                                 765
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
                        775
                                            780
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                    790
                                        795
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                805
                                    810
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
            820
                                825
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        835
                            840
                                                845
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
                        855
                                            860
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                    870
                                        875
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                885
                                    890
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                                905
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
                            920
                                                 925
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
                        935
                                            940
Leu Ser Leu Ser Pro Gly Lys
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      <213> Homo sapiens
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Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser

<400> 10

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Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
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Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
                       55
Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
                   70
                                       75
Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
               85
                                   90
Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
                               105
Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
                           120
Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
                       135
                                           140
Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
                   150
                                       155
Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg
               165
                                   170
Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val
                               185
                                                   190
Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr
                           200
                                               205
Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro
                       215
                                           220
Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu
                   230
                                       235
Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys
               245
                                  250
Tyr Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser Thr Trp Ser Gln Ile
           260
                               265
                                     . 270
Pro Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser Phe Thr Val Gln Asp
                           280
                                              285
Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu
                       295
                                           300
Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile
                                       315
                   310
Thr Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser Gly
               325
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<210> 11

<211> 120

<212> PRT

<213> Homo sapiens

<400> 11

Ser Gly Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys 10 1 Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly 2.5 Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro 4.0 Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr 55 60 Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val 70 75 Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn 90 Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro 105 100 Lys Ser Cys Asp Lys Thr His Thr

<210> 12
<211> 329
<212> PRT
<213> Homo sapiens

<400> 12

Ser Gly Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys
1 5 10 15

Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys

10 Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys 25 Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu 40 Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu 55 60 Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Leu Gly Thr 70 75 Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val 90 85 Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro 1.05 1.00 110 Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys 120 125 Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val 135 140 Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr 150 155 Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu 165 170 Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His 190 180 185 Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys 195 200 205 Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln 215 220 Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Met 230 235 Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro 245 250 Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn 265 260 Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu 275 280 Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val 295 300 Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln 310 315 Lys Ser Leu Ser Leu Ser Leu Gly Lys

<210> 13 <211> 108 <212> PRT

325

<213> Homo sapiens

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu 40 Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp 5.5 Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser 85 Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 100 <210> 14 <211> 106 <212> PRT <213> Homo sapiens <400> 14 Ser Gly Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser 10 Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp 25 20 Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro 40 45 Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn

 Phe
 Tyr
 Pro
 Gly
 Ala
 Val
 Thr
 Val
 Ala
 Trp
 Lys
 Ala
 Asp
 Ser
 Ser
 Pro

 Val
 Lys
 Ala
 Gly
 Val
 Glu
 Thr
 Thr
 Thr
 Pro
 Ser
 Lys
 Gln
 Ser
 Asn
 Asn

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser 100 105

> <210> 15 <211> 360 <212> PRT

<400> 15

<213> Homo sapiens

165

Met Val Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro 40 Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys 55 60 Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg 75 70 Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys 85 90 Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val 105 Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser 120 Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr 135 140 Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp 150 155

Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys

Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met

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185
                                                    190
            180
Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe
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                                                205
Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val
                                            220
                       215
Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp
                   230
                                        235
Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg
                                   250
                245
Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp
                                265
Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His
                           280
                                                285
Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser
                        295
                                            300
Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser
                    310
                                        315
Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr
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                                    330
Asn Lys Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr
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Ser Leu Pro Val Gln Asp Ala Gly
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Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro
                            40
Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys
                        5.5
Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg
                    70
                                        .75
Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys
                                    90
                85
Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val
            100
                                105
Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser
                            120
        115
Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr
                        135
                                            140
Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp
                                        155
                    150
Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys
                165
                                    170
Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met
                                185
                                                    190
Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe
                            200
Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val
                        215
                                            220
Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp
                                        235
                    230
Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg
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Tyr	Arg	Ala	Glu	245 Arg	Ser	Lys	Thr	Phe	250 Thr	Thr	Trp	Met	Val	255 Lys	Asp		
Leu	Gln		260 His	Cys	Val	Ile		265 Asp	Ala	Trp	Ser		270 Leu	Arg	His		
Val		275 Gln	Leu	Arg	Ala		280 Glu	Glu	Phe	Gly		285 Gly	Glu	Trp	Ser	·	
Glu 305	290 Trp	Ser	Pro	Glu	Ala 310	295 Met	Gly	Thr	Thr	Gly 315	300						
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	<2	220> 221> 222>		(2	2082)	ı											
_	gtg	_	cca		tta Leu												48
					Gl <sup>A</sup> aaa												96
					gct Ala												144
					act Thr												192
		_			atg Met 70		_				-	_					240
					act Thr												288
					tgc Cys												336
					caa Gln												384
_	_	_		_	gac Asp			-									432
_			_	_	aat Asn 150	_					_						480
aca	ctt	cac	aaa	ctg	agt	gaa	tcc	cag	cta	gaa	ctg	aac	tgg	aac	aac		528

Thr	Leu	His	Lys	Leu 165	Ser	Glu	Ser	Gln	Leu 170	Glu	Leu	Asn	Trp	Asn 175	Asn	
								cac His 185								576
								tca Ser								624
tcc Ser	ttg Leu 210	cct Pro	agt Ser	gtg Val	gat Asp	ggg Gly 215	cag Gln	aaa Lys	cgc Arg	tac Tyr	acg Thr 220	ttt Phe	cgt Arg	gtt Val	cgg Arg	672
agc Ser 225	cgc Arg	ttt Phe	aac Asn	cca Pro	ctc Leu 230	tgt Cys	gga Gly	agt Ser	gcț Ala	cag Gln 235	cat His	tgg Trp	agt Ser	gaa Glu	tgg Trp 240	720
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					ctg Leu												1152
					cat His 390												1200
					ttc Phe												1248
					gcc Ala												1296
					tgg Trp												1344
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					tca Ser												1488
					cgg Arg												1536
					cct Pro												1584
					gcc Ala												1632
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ctg Leu	aat Asn	ggc Gly	aag Lys	gag Glu 565	tac Tyr	aag Lys	tgc, Cys	aag Lys	gtc Val 570	tcc Ser	aac Asn	aaa Lys	gcc Ala	ctc Leu 575	cca Pro		1728
				Lys	acc Thr												1776

cca																
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	gtg Val															1920
	cct Pro															1968
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Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe 195 200 205

Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro Thr Cys Val Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met Asn Gly Pro Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu Val Phe Leu Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly Gly Ala Gly Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala Asp Asn Tyr Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys Gly Ser Phe Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn Leu Thr Val His Thr Asn Val Ser Asp Thr Leu Leu Thr Trp Ser Asn Pro Tyr Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala Val Asn Ile Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn Val Thr Tyr Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys Ser Gly Ile Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Ser Tyr Asn Thr Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser Tyr Arg Glu Pro Phe Glu Gln Ser Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

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													tat Tyr			288
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													ccc Pro			384
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Cys	Val	Ala 195	Ser	Ser	Val	Gly	Ser 200	Lys	Phe	Ser	Lys	Thr 205	Gln	Thr	Phe	
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	gcc Ala															720
	cac His															768
	cgg Arg															816
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	gtg Val 290															912
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	cca Pro															1008
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	tgg Trp															1200
	aac Asn															1248
	att Ile															1296
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			gaa Glu 470						1440
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			act Thr						1536
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			cca Pro						1728
			acc Thr						1776
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			ggc						2016
			gcc Ala						2064

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Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys Tyr Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser Thr Trp Ser Gln Ile Pro Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser Phe Thr Val Gln Asp Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile Thr Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser Phe Trp Tyr Lys Ile Asp Pro Ser His Thr Gln Gly Tyr Arg Thr Val Gln Leu Val Trp Lys Thr Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile Leu Asp Tyr Glu Val Thr Leu Thr Arg Trp Lys Ser His Leu Gln Asn Tyr Thr Val Asn Ala Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Leu Ala Thr Leu Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile Pro Ala Cys Asp Phe Gln Ala Thr His Pro Val Met Asp Leu Lys Ala Phe Pro Lys Asp Asn Met Leu Trp Val Glu Trp Thr Thr Pro Arg Glu Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala Pro Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly Thr Val His Arg Thr Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser Ile Lys Ala Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val Arg Thr Lys Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln Leu Pro Val Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe Tyr Arg Thr Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser His Thr Glu Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met Val Arg Met Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu Phe Thr Phe Thr

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Thr Pro Lys 930	Phe Ala		Gly 935		Ile	Glu	Ser	Gly 940	Gly	Asp	Lys	Thr	
His Thr Cys 945	Pro Pro	Cys 950	Pro	Ala	Pro	Glu	Leu 955	Leu	Gly	Gly	Pro	Ser 960	
Val Phe Leu	Phe Pro		Lys	Pro	Lys	Asp 970	Thr	Leu	Met	Ile	Ser 975	Arg	
Thr Pro Glu	Val Thr 980	Cys	Val	Val	Val 985	Asp	Val	Ser	His	Glu 990	Asp	Pro	
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Lys Cys Lys	Val Ser	Asn		Ala	Leu	Pro 1050		Pro	Ile	Glu	Lys 1055		
Ile Ser Lys			Gln	Pro	Arg 1065	Glu		Gln	Val	Tyr 1070		Leu	
Pro Pro Ser	Arg Asp	Glu	Leu	Thr 1080	Lys		Gln	Val	Ser 1085		Thr	Cys	
Leu Val Lys			Pro 1095	Ser		Ile	Ala	Val 1100	Glu		Glu	Ser	
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Ser Asp Gly	Ser Phe	Phe		Tyr	Ser	Lys 1130	Leu		Val	Asp	Lys 1139		
Arg Trp Gln			Val	Phe	Ser 1145		Ser	Val	Met	His 1150		Ala	
Leu His Asn	His Tyr	Thr	Gln			Leu	Ser	Leu			Gly	Lys	
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1 Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser M 185
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aca aca tgg atg gtc aag g Thr Thr Trp Met Val Lys A 270  gcc tgg agc ggc ctg agg c Ala Trp Ser Gly Leu Arg H 285
gag ttc ggg caa ggc gag tgg a Slu Phe Gly Gln Gly Glu Trp S 300 acg cct tgg aca gaa tcg cga t Thr Pro Trp Thr Glu Ser Arg S 315

cct Pro	cca Pro	gct Ala	gag Glu	aac Asn 325	gag Glu	gtg Val	tcc Ser	acc Thr	ccc Pro 330	atg Met	gaa Glu	ctt Leu	cta Leu	gac Asp 335	cca Pro	1008
								cca Pro 345								1056
								gaa Glu								1104
								aaa Lys								1152
								aga Arg		_		_	_			1200
								cag Gln			_					1248
								tat Tyr 425								1296
								ttg Leu								1344
								ggt Gly			-			_		1392
								tgg Trp								1440
								acc Thr								1488
								gtc Val 505								1536
								atc Ile								1584
								tta Leu								1632
								tgg Trp								1680
gtt	ata	ata	cta	aaa	tat	aac	att	caa	tat	agg	acc	aaa	gat	gcc	tca	1728

Val	Ile	Ile	Leu	Lys 565	Tyr	Asn	Ile	Gln	Tyr 570	Arg	Thr	Lys	Asp	Ala 575	Ser	
	tgg Trp								Thr							1776
	act Thr															1824
	tgt Cys 610															1872
gaa Glu 625	gca Ala	agt Ser	gly ggg	atc Ile	acc Thr 630	tat Tyr	gaa Glu	gat Asp	aga Arg	cca Pro 635	tct Ser	aaa Lys	gca Ala	cca Pro	agt Ser 640	1920
	tgg Trp															1968
	ctc Leu															2016
	gat Asp															2064
	aca Thr 690														cgc Arg	2112
	cta Leu															2160
gct Ala	gtt Val	tta Leu	act Thr	atc Ile 725	cct Pro	gcc Ala	tgt Cys	gac Asp	ttt Phe 730	caa Gln	gct. Ala	act Thr	cac His	cct Pro 735	gta Val	2208
atg Met	gat Asp	ctt Leu	aaa Lys 740	gca Ala	ttc Phe	ccc Pro	aaa Lys	gat Asp 745	aac Asn	atg Met	ctt Leu	tgg Trp	gtg Val 750	gaa Glu	tgg Trp	2256
	act Thr															2304
tta Leu	tca Ser 770	gat Asp	aaa Lys	gca Ala	ccc Pro	tgt Cys 775	atc Ile	aca Thr	gac Asp	tgg Trp	caa Gln 780	caa Gln	gaa Glu	gat Asp	ggt Gly	2352
	gtg Val															2400
tat Tyr	ttg Leu	ata Ile	aca Thr	gtt Val	act Thr	cca Pro	gta Val	tat Tyr	gct Ala	gat Asp	gga Gly	cca Pro	gga Gly	agc Ser	cct Pro	2448

				805					810		,			815		
			aag Lys 820													2496
			aca Thr													2544
			cct Pro													2592
			aga Arg													2640
			aca Thr													2688
			cga Arg 900													2736
			act Thr													2784
			gac Asp													2832
			gga Gly													2880
			atc Ile													2928
gtg Val	agc Ser	cac His	gaa Glu 980	gac Asp	cct Pro	gag Glu	gtc Val	aag Lys 985	ttc Phe	aac Asn	tgg Trp	tac Tyr	gtg Val 990	gac Asp	ggc Gly	2976
gtg Val	gag Glu	gtg Val 99	His	aat Asn	gcc Ala	aag Lys	aca Thr 100	Lys	ccg Pro	cgg Arg	gag Glu	gag Glu 100	Gln	tac Tyr	aac Asn	3024
agc Ser	acg Thr 101	Tyr	cgt Arg	gtg Val	gtc Val	agc Ser 101	Val	ctc Leu	acc Thr	gtc Val	ctg Leu 102	His	cag Gln	gac Asp	tgg Trp	3072
ctg Leu 102	Asn	ggc Gly	aag Lys	gag Glu	tac Tyr 103	Lys	tgc Cys	aag Lys	gtc Val	tcc Ser 103	Asn	aaa Lys	gcc Ala	ctc Leu	cca Pro 1040	3120
gcc Ala	ccc Pro	atc Ile	gaġ Glu	aaa Lys 104	Thr	atc Ile	tcc Ser	aaa Lys	gcc Ala 105	Lys	Gly aaa	cag Gln	ccc Pro	cga Arg 105	Glu	3168

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac	
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn 1060 1065 1070	3216
cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile 1075 1080 1085	3264
gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr 1090 1095 1100	3312
acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys 1105 1110 1115 1120	3360
ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys 1125 1130 1135	3408
tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu 1140 1145 1150	3456
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1 5 10 15  Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg 20 25 30  Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro	
1 5 10 15  Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg 20 25 30  Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro 35 40 45  Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys	
1	
1	
1	
1	
1	
1	
1	
1	

		195					200					205			
Gln	Gly 210	Cys	Gly	Ile	Leu	Gln 215	Pro	Asp	Pro	Pro	Ala 220	Asn	Ile	Thr	Val
Thr 225	Ala	Val	Ala	Arg	Asn 230	Pro <sub>.</sub>	Arg	Trp	Leu	Ser 235	Val	Thr	Trp	Gln	Asp 240
Pro	His	Ser	Trp	Asn 245		Ser	Phe	Tyr	Arg 250	Leu	Arg	Phe	Glu	Leu 255	Arg
Tyr	Arg	Ala	Glu 260	Arġ	Ser	Lys	Thr	Phe 265	Thr	Thr	Trp	Met	Val 270	Lys	Asp
Leu	Gln	His 275	His	Cys	Val	Ile	His 280	Asp	Ala	Trp	Ser	Gly 285	Leu	Arg	His
Val	Val 290	Gln	Leu	Arg	Ala	Gln 295	Glu	Glu	Phe	Gly	Gln 300	Gly	Glu	Trp	Ser
Glu 305	Trp	Ser	Pro	Glu	Ala 310	Met	Gly	Thr	Pro	Trp 315	Thr	Glu	Ser	Arg	Ser 320
Pro	Pro	Ala	Glu	Asn 325	Glu	Val	Ser	Thr	Pro 330	Met	Glu	Leu	Leu	Asp 335	Pro
Cys	Gly	Tyr	Ile 340	Ser	Pro	Glu	Ser	Pro 345	Val	Val	Gln	Leu	His 350	Ser	Asn
Phe	Thr	Ala 355	Val	Cys	Val	Leu	Lys 360	Glu	Lys	Суѕ	Met	Asp 365	Tyr	Phe	His
Val	Asn 370	Ala	Asn	Tyr	Ile	Val 375	Trp	Lys	Thr	Asn	His 380	Phe	Thr	Ile	Pro
Lys 385	Glu	Gln	Tyr	Thr	Ile 390	Ile	Asn	Arg	Thr	Ala 395	Ser	Ser	Val	Thr	Phe 400
Thr	Asp	Ile	Ala	Ser 405	Leu	Asn	Ile	Gln	Leu 410	Thr	Сув	Asn	Ile	Leu 415	Thr
Phe	Gly	Gln	Leu 420	Glu	Gln	Asn	Val	Tyr 425	Gly	Ile	Thr	Ile	Ile 430	Ser	Gly
		435	Glu				440					445			
	450		Arg			455					460				
465			Thr		470					475					480
			Lys	485					490					495	
			Phe 500	•				505					510		
		515	Val				520					525			
	530					535					540				Glu
545					550					555					Ser 560
			Leu	565					570					575	
			580					585					590		Ser
		595					600					605			Ile
	610		Lys			615					620				
625					630					635					Ser 640
	_	_	Lys	645					650					655	
			660					665					670		Ile
Leu	Asp	Туг 675	Glu	Val	Thr	Leu	Thr 680	Arg	Trp	Lys	Ser	His 685	Leu	Gln	Asn

Tyr Thr Val Asn Ala Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Leu Ala Thr Leu Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile Pro Ala Cys Asp Phe Gln Ala Thr His Pro Val Met Asp Leu Lys Ala Phe Pro Lys Asp Asn Met Leu Trp Val Glu Trp Thr Thr Pro Arg Glu Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala Pro Cys Ile Thr Asp Trp Gln Glu Asp Gly Thr Val His Arg Thr Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser Ile Lys Ala Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val Arg Thr Lys Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln Leu Pro Val Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe Tyr Arg Thr Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser His Thr Glu Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met Val Arg Met Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu Phe Thr Phe Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro 1025 1030 Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 

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	<2	220> 221> 222>	CDS (1)	(2	2730)	ı								·
_	gtg		ctg		_	_		agt Ser					_	48
	-	_	_		_	_	_	gat Asp 25	_			_	_	96
								gag Glu						144
								aac Asn						192
								act Thr						240
								gag Glu						288
								ctc Leu 105						336
	_	_						tat Tyr	_	_	_	_		384
								tgt Cys						432
								tat Tyr						480
								tcc Ser						528
		_		-				cag Gln 185						576
-		_		_	_			att Ile	_					624

aat Asn	tac Tyr 210	aca Thr	tgt Cys	gtt Val	gtt Val	aca Thr 215	tat Tyr	cca Pro	gaa Glu	aat Asn	gga Gly 220	cgt Arg	acg Thr	ttt Phe	cat His	672
					act Thr 230											720
					cat His											768
					cta Leu											816
ctg Leu	atg Met	gat Asp 275	tct Ser	cgc Arg	aat Asn	gag Glu	gtt Val 280	tgg Trp	tgg Trp	acc Thr	att Ile	gat Asp 285	gga Gly	aaa Lys	aaa Lys	864
					att Ile											912
agt Ser 305	aga Arg	aca Thr	gaa Glu	gat Asp	gaa Glu 310	aca Thr	aga Arg	act Thr	cag Gln	att Ile 315	ttg Leu	agc Ser	atc Ile	aag Lys	aaa Lys 320	960
gtt Val	acc Thr	tct Ser	gag Glu	gat Asp 325	ctc Leu	aag Lys	cgc Arg	agc Ser	tat Tyr 330	gtc Val	tgt Cys	cat His	gct Ala	aga Arg 335	agt Ser	1008
					gcc Ala											1056
gct Ala	cca Pro	aga Arg 355	tac Tyr	aca Thr	gtg Val	tcc Ser	ggt Gly 360	ggc Gly	gcg Ala	cct Pro	atg Met	ctg Leu 365	agc Ser	gag Glu	gct Ala	1104
gat Asp	aaa Lys 370	tgc Cys	aag Lys	gaa Glu	cgt Arg	gaa Glu 375	gaa Glu	aaa Lys	ata Ile	att Ile	tta Leu 380	gtg Val	tca Ser	tct Ser	gca Ala	1152
					cgt Arg 390											1200
ggc Gly	act Thr	ata Ile	act Thr	tgg Trp 405	tat Tyr	aag Lys	gat Asp	gac Asp	agc Ser 410	aag Lys	aca Thr	cct Pro	gta Val	tct Ser 415	aca Thr	1248
				Arg	att Ile											1296
			Val		gat Asp											1344

					aga Arg											1392
					tat Tyr 470				Ala							1440
					gga Gly											1488
					gag Glu											1536
					gac Asp											1584
					gtg Væl											1632
					tac Tyr 550											1680
					cta Leu											1728
					gag Glu											1776
					gtc Val											1824
					gta Val											1872
					gaa Glu 630									Thr	ctc Leu 640	1920
atc Ile	aca Thr	gtg Val	ctt Leu	aat Asn 645	ata Ile	tcg Ser	gaa Glu	att Ile	gag Glu 650	agt Ser	aga Arg	ttt Phe	tat Tyr	aaa Lys 655	cat His	1968
					gcc Ala											2016
					cca Pro											2064
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Cys	Pro 690	Pro	Cys	Pro	Ala	Pro 695	Glu	Leu	Leu	Gly	Gly 700	Pro	Ser	Val	Phe	
											atc Ile					2160
											gaa Glu					2208
											cat His					2256
aag Lys	ccg Pro	cgg Arg 755	gag Glu	gag Glu	cag Gln	tac Tyr	aac Asn 760	agc Ser	acg Thr	tac Tyr	cgt Arg	gtg Val 765	gtc Val	agc Ser	gtc Val	2304
											aag Lys 780					2352
aag Lys 785	gtc Val	tcc Ser	aac Asn	aaa Lys	gcc Ala 790	ctc Leu	cca Pro	gcc Ala	ccc Pro	atc Ile 795	gag Glu	aaa Lys	acc Thr	atc Ile	tcc Ser 800	2400
aaa Lys	gcc Ala	aaa Lys	Gly ggg	cag Gln 805	ccc Pro	cga Arg	gaa Glu	cca Pro	cag Gln 810	gtg Val	tac Tyr	acc Thr	ctg Leu	ccc Pro 815	cca Pro	2448
				Met							ctg Leu					2496
aaa Lys	ggc Gly	ttc Phe 835	tat Tyr	ccc Pro	agc Ser	,gac Asp	atc Ile 840	gcc Ala	gtg Val	gag Glu	tgg Trp	gag Glu 845	agc Ser	aat Asn	ggg Gly	2544
cag Gln	ccg Pro 850	gag Glu	aac Asn	aac Asn	tac Tyr	aag Lys 855	acc Thr	acg Thr	cct Pro	ccc Pro	gtg Val 860	ctg Leu	gac Asp	tcc Ser	gac Asp	2592
											gac Asp					2640
cag Gln	cag Gln	Gly aaa	aac Asn	gtc Val 885	ttc Phe	tca Ser	tgc Cys	tcc Ser	gtg Val 890	atg Met	cat His	gag Glu	gct Ala	ctg Leu 895	cac His	2688
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tga			0.5													2733
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<sup>&</sup>lt;210> 28

<sup>&</sup>lt;211> 910

<sup>&</sup>lt;212> PRT <213> Homo sapiens

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475
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465
                   470
Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro Tyr Met Glu Phe Phe
               485
                                  490
Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln Trp Tyr Lys Asp Cys
                              505
          500
Lys Pro Leu Leu Asp Asn Ile His Phe Ser Gly Val Lys Asp Arg
                       520 ·
Leu Ile Val Met Asn Val Ala Glu Lys His Arg Gly Asn Tyr Thr Cys
                      535 · ·
His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr Pro Ile Thr Arg Val
                                      555
                   550
Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro Thr Arg Pro Val Ile
               565
                                  570
Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp Leu Gly Ser Gln Ile
        . 580
                               585
Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser Asp Ile Ala Tyr Trp
                                              605
       595
                           600
Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp Pro Val Leu Gly Glu
                       615
                                          620
Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys Arg Arg Ser Thr Leu
                                       635
                   630
Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser Arg Phe Tyr Lys His
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                                   650
Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly Ile Asp Ala Ala Tyr
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                              665
Ile Gln Leu Ile Tyr Pro Val Thr Asn Ser Gly Asp Lys Thr His Thr
                          680
Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
                       695
                                           700
Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
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                                      715
Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
               725
                                   730
Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
                               745
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
                           760
       755
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
                       775
                                           780
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                    790
                                       795
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
               805
                                   810
Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
            820
                               825
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
        835
                           840
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
                       855
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                   870
                                       875
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
                               890
               885
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                               905
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<sup>&</sup>lt;210> 29

<sup>&</sup>lt;211> 2355

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

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	ctg Leu															96
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	ggt Gly 50															192
	ttt Phe															240
ggc	gcg Ala	ggg ggg	tgc Cys	gtg Val 85	tgc Cys	cac His	ctg Leu	ctc Leu	atg Met 90	gat Asp	gac Asp	gtg Val	gtc Val	agt Ser 95	gcg Ala	288
	aac Asn															336
	tcc Ser															384
	aca Thr 130															432
	ccg Pro															480
gtc Val	aac Asn	att Ile	tgg Trp	agt Ser 165	gaa Glu	aac Asn	gac Asp	ccg Pro	gca Ala 170	gat Asp	ttc Phe	aga Arg	atc Ile	tat Tyr 175	aac Asn	528
	acc Thr															576
tct Ser	ggg Gly	att Ile 195	tcc Ser	tac Tyr	agg Arg	gca Ala	cgg Arg 200	gtg Val	agg Arg	gcc Ala	tgg Trp	gct Ala 205	cag Gln	agc Ser	tat Tyr	624
aac Asn	acc Thr 210	acc Thr	tgg Trp	agt Ser	gag Glu	tgg Trp 215	agc Ser	ccc Pro	agc Ser	acc Thr	aag Lys 220	tgg Trp	cac His	aac Asn	tcc Ser	672

					gag Glu 230											720
					cct Pro											768
	_		_		tgg Trp											816
					tat Tyr											864
					act Thr											912
					gtg Val 310											960
					gtt Val											1008
					act Thr											1056
					tgg Trp											1104
					tat Tyr											1152
					aga Arg 390											1200
ctg Leu	acc Thr	aaa Lys	gtg Val	aag Lys 405	gat Asp	tcc Ser	agt Ser	ttt Phe	gaa Glu 410	caa Gln	cac His	agt Ser	gtc Val	caa Gln 415	ata Ile	1248
					gca Ala											1296
					gtg Val											1344
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ttt	att	agc	aga	tgc	cta	ttt	tat	gaa	gta	gaa	gtc	aat	aac	agc	caa	1440

465	Ile	Ser	Arg	Cys	Leu 470	Phe	Tyr	Glu	Val	Glu 475	Val	Asn	Asn	Ser	Gln 480	
					_			_			_		_	gag Glu 495		1488
	-			_							-		_	gtc Val		1536
	•			~		_			_	_		_	_	aaa Lys		1584
	_		-			-	-				-			agc Ser		1632
_	_	-			_	_	_						_	aaa Lys		1680
		_		_	_		_		_		-			ccg Pro 575		1728
-								_	_			_		tcc Ser		1776
		-	-		_				_		-		_	gac Asp		1824
		595					600					605				
	gtc	aag	ttc	aac			gtg					gtg		aat Asn	gcc	1872
Glu aag	gtc Val 610 aca	aag Lys aag	ttc Phe ccg	aac Asn cgg	Trp	Tyr 615 gag	gtg Val cag	Asp	Gly	Val	Glu 620 acg	gtg Val tac	His cgt		gcc Ala gtc	1872 1920
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•	675			680					685			
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